EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2	"2040145".pn.	US-PGPUB; USPAT; EPO	OR	ON	2006/04/03 07:16
L2	179	"methacholine chloride" and acetate and "sodium chloride"	US-PGPUB; USPAT; EPO	OR	ON	2006/04/03 07:17
L3	119	"methacholine chloride" same acetate and "sodium chloride"	US-PGPUB; USPAT; EPO	OR	ON	2006/04/03 07:41
L4	0	"methacholine chloride" same acetate.ti,ab. and "sodium chloride"	US-PGPUB; USPAT; EPO	OR	ON	2006/04/03 07:17
L5	172	"methacholine chloride" same acetate	US-PGPUB; USPAT; EPO	OR	ON	2006/04/03 07:41
S1	1204	methacholine	US-PGPUB; USPAT; EPO	OR	ON	2006/04/03 07:01
S2	1	methacholine.ti.	US-PGPUB; USPAT; EPO	OR	ON	2006/03/20 20:20
S3	7	methacholine.ti,ab.	US-PGPUB; USPAT; EPO	OR	ON	2006/03/20 20:23
S4	0	"methacholine chloride".ti,ab.	US-PGPUB; USPAT; EPO	OR	ON	2006/03/20 20:23
S5	315	"methacholine chloride"	US-PGPUB; USPAT; EPO	OR	ON	2006/03/20 20:26
S6	1	"methacholine chloride" with treatment	US-PGPUB; USPAT; EPO	OR	ON	2006/03/20 20:26
S7	1	"4,933,165".pn.	US-PGPUB; USPAT; EPO	OR	ON	2006/03/21 10:39
S8	264	lipitor	US-PGPUB; USPAT; EPO	OR	ON	2006/03/21 10:39
S9	0	lipitor.ti.	US-PGPUB; USPAT; EPO	OR	ON	2006/03/21 10:39
S10	0	"lipitor.ti,ab.."	US-PGPUB; USPAT; EPO	OR	ON	2006/03/21 10:51

EAST Search History

S11	1	"4,681,893".pn.	US-PGPUB; USPAT; EPO	OR	ON	2006/03/21 10:52
S12	1	"6121319".pn.	US-PGPUB; USPAT; EPO	OR	ON	2006/03/21 10:52

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Connecting via Winsock to STN


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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  DEC 21   IPC search and display fields enhanced in CA/CAplus with the
                   IPC reform
 NEWS  4  DEC 23   New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
                   USPAT2
 NEWS  5  JAN 13   IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
 NEWS  6  JAN 13   New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
                   INPADOC
 NEWS  7  JAN 17   Pre-1988 INPI data added to MARPAT
 NEWS  8  JAN 17   IPC 8 in the WPI family of databases including WPIFV
 NEWS  9  JAN 30   Saved answer limit increased
 NEWS 10  JAN 31   Monthly current-awareness alert (SDI) frequency
                   added to TULSA
 NEWS 11  FEB 21   STN AnaVist, Version 1.1, lets you share your STN AnaVist
                   visualization results
 NEWS 12  FEB 22   Status of current WO (PCT) information on STN
 NEWS 13  FEB 22   The IPC thesaurus added to additional patent databases on STN
 NEWS 14  FEB 22   Updates in EPFULL; IPC 8 enhancements added
 NEWS 15  FEB 27   New STN AnaVist pricing effective March 1, 2006
 NEWS 16  FEB 28   MEDLINE/LMEDLINE reload improves functionality
 NEWS 17  FEB 28   TOXCENTER reloaded with enhancements
 NEWS 18  FEB 28   REGISTRY/ZREGISTRY enhanced with more experimental spectral
                   property data
 NEWS 19  MAR 01   INSPEC reloaded and enhanced
 NEWS 20  MAR 03   Updates in PATDPA; addition of IPC 8 data without attributes
 NEWS 21  MAR 08   X.25 communication option no longer available after June 2006
 NEWS 22  MAR 22   EMBASE is now updated on a daily basis

 NEWS EXPRESS  FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
               V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
               http://download.cas.org/express/v8.0-Discover/

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FILE 'HOME' ENTERED AT 07:41:15 ON 03 APR 2006

=> s "methacholine chloride" (L) acetate
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

=> file medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 07:41:41 ON 03 APR 2006

 FILE LAST UPDATED: 1 APR 2006 (20060401/UP).  FILE COVERS 1950 TO DATE.

 On December 11, 2005, the 2006 MeSH terms were loaded.

 The MEDLINE reload for 2006 is now (26 Feb.) available.  For details
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

 OLDMEDLINE is covered back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s "methacholine chloride" (L) acetate
          7710 "METHACHOLINE"
        145706 "CHLORIDE"
          3807 "METHACHOLINE CHLORIDE"
                 ("METHACHOLINE"(W)"CHLORIDE")
         97995 ACETATE
L1           1 "METHACHOLINE CHLORIDE" (L) ACETATE

=> d

L1   ANSWER 1 OF 1     MEDLINE on STN
AN   1998302161     MEDLINE
DN   PubMed ID: 9638314
TI   Synergistic effects of ularitide acetate with classical bronchorelaxants
     on guinea-pig tracheal smooth muscle.
AU   Korn C; Neidlein R; Strein K; Wilhelms O H
CS   Pharmaceutical-Chemical Institute, University of Heidelberg, Germany.
SO   Arzneimittel-Forschung, (1998 May) Vol. 48, No. 5, pp. 475-81.
     Journal code: 0372660. ISSN: 0004-4172.
CY   GERMANY: Germany, Federal Republic of
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   199807
ED   Entered STN: 19980723
     Last Updated on STN: 19990129
     Entered Medline: 19980716
```

```
=> s l1
          7710 "METHACHOLINE"
        145706 "CHLORIDE"
          3807 "METHACHOLINE CHLORIDE"
                 ("METHACHOLINE"(W)"CHLORIDE")
         97995 ACETATE
L2           1 "METHACHOLINE CHLORIDE" (L) ACETATE

=> d abs

L2   ANSWER 1 OF 1     MEDLINE on STN
AB   Ularitide (CAS 118812-69-4, urodilatin) is a member of the family of the
     atrial natriuretic peptides.  In the present study, the relaxant effects
     of ularitide acetate, isoproterenol (isoprenaline) hemisulfate,
     aminophylline, zaprinast, and different combinations between these drugs
     were investigated on methacholine chloride
     -precontracted guinea-pig tracheal smooth muscle.  Ularitide
     acetate was a weaker bronchorelaxant than isoproterenol
     hemisulfate and aminophylline.  Moreover the relaxation induced by
     ularitide acetate was reversible, while the relaxation induced
     by isoproterenol hemisulfate, aminophylline, and zaprinast was
     irreversible.  Combinations between in each case two of these substances
     were overadditive, if the phosphodiesterase-inhibiting component was
     applicated before the combination partner.  Their effects were only
     additive, if the combination partners were applicated simultaneously.  All
     combinations between ularitide acetate and isoproterenol
     hemisulfate, aminophylline, or zaprinast respectively relaxed the tracheas
     irreversibly.  These results suggest that ularitide acetate
     might be a novel partner for classical bronchorelaxants in potent
     bronchorelaxing combinations in the therapy of asthma bronchiale.


=> s "methacholine chloride" and acetate
          7710 "METHACHOLINE"
        145706 "CHLORIDE"
          3807 "METHACHOLINE CHLORIDE"
                 ("METHACHOLINE"(W)"CHLORIDE")
         97995 ACETATE
L3          25 "METHACHOLINE CHLORIDE" AND ACETATE

=> d 1-25 bib abs

L3   ANSWER 1 OF 25     MEDLINE on STN
AN   2006001297     MEDLINE
DN   PubMed ID: 16324695
TI   Protein kinase C potentiates homologous desensitization of the
     beta2-adrenoceptor in bovine tracheal smooth muscle.
AU   Boterman Mark; Smits Steven R J G; Meurs Herman; Zaagsma Johan
CS   Department of Molecular Pharmacology, University Centre for Pharmacy, A.
     Deusinglaan 1, 9713 AV Groningen, The Netherlands.. M.Boterman@rug.nl
SO   European journal of pharmacology, (2006 Jan 4) Vol. 529, No. 1-3, pp.
     151-6.  Electronic Publication: 2005-12-01.
     Journal code: 1254354. ISSN: 0014-2999.
CY   Netherlands
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200603
ED   Entered STN: 20060104
     Last Updated on STN: 20060310
     Entered Medline: 20060309
AB   Preincubation (30 min) of bovine tracheal smooth muscle with various
     concentrations (0.1, 1 and 10 microM) of fenoterol decreased
     isoprenaline-induced maximal relaxation (E(max)) of methacholine-
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contracted preparations in a concentration dependent fashion, indicating desensitization of the beta(2)-adrenoceptor. Preincubation with 1 microM of the protein kinase C (PKC) activator phorbol 12-myristate 13-**acetate** (PMA) caused a small but significant decrease in isoprenaline-induced E(max), indicating activated PKC-mediated heterologous beta(2)-adrenoceptor desensitization. To investigate the capacity of activated PKC to regulate homologous desensitization, we incubated the smooth muscle strips with the combination of both 1 microM PMA and 1 microM fenoterol. This combined treatment synergistically decreased the isoprenaline-induced maximal relaxation, as compared to the individual effects of PMA and fenoterol alone, indicating a common pathway for heterologous and homologous desensitization. Moreover, the specific PKC-inhibitor 2-[1-(3-dimethylaminopropyl)-1H-indol-3-yl]-3-(1H-indol-3-yl) maleimide (GF 109203X) markedly increased the potency and E(max) of isoprenaline for all conditions used, including control conditions, and the synergistic effects of PMA and fenoterol were completely prevented. In conclusion, the present study demonstrates that homologous desensitization of the beta(2)-adrenergic receptor can be enhanced by PKC activation. For the first time we have provided evidence that this concept is functionally operative in airway smooth muscle, and it may explain the reduced bronchodilator response to beta(2)-adrenoceptor agonists in patients with asthma during a severe exacerbation.

L3 ANSWER 2 OF 25 MEDLINE on STN
AN 2005316134 MEDLINE
DN PubMed ID: 15840578
TI Role of alpha1 2.3 subunit I-II linker sites in the enhancement of Ca(v) 2.3 current by phorbol 12-myristate 13-**acetate** and acetyl-beta-methylcholine.
AU Fang Hongyu; Franke Ruthie; Patanavanich Saharat; Lalvani Amrita; Powell Natalie K; Sando Julianne J; Kamatchi Ganesan L
CS Department of Anesthesiology, University of Virginia Health Sciences Systems, Charlottesville, Virginia 22908, USA.
NC GM31184 (NIGMS)
GM65214 (NIGMS)
SO The Journal of biological chemistry, (2005 Jun 24) Vol. 280, No. 25, pp. 23559-65. Electronic Publication: 2005-04-19.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200509
ED Entered STN: 20050621
Last Updated on STN: 20050930
Entered Medline: 20050929
AB Potentiation of Ca(v) 2.3 currents by phorbol 12-myristate 13-**acetate** (PMA) or acetyl-beta-methylcholine (MCh) may be due to protein kinase C (PKC)-mediated phosphorylation of the alpha1 2.3 subunit. Mutational analysis of potential PKC sites unique to the alpha1 2.3 subunit revealed several sites in the II-III linker that are specific to MCh (Kamatchi, G., Franke, R., Lynch, C., III, and Sando, J. (2004) J. Biol. Chemical 279, 4102-4109). To identify sites responsive to PMA, Ser/Thr --> Ala mutations were made in potential PKC sites homologous to the alpha1 2.3 and 2.2 subunits, both of which respond to PMA. Wild type alpha1 2.3 or mutants were expressed in Xenopus oocytes in combination with beta1b and alpha2/delta subunits and muscarinic M1 receptors. Inward current (I(Ba)) was recorded using Ba2+ as the charge carrier. Thr-365 of the I-II linker was identified as the primary site of PMA action, and this site also was required, along with the previously identified MCh-selective sites, for the MCh response. Ser-369 and Ser-1995 contributed to current enhancement only if Thr-365 also was available. Mutation of the essential sites to Asp increased the basal I(Ba) and caused a corresponding decrease in the PMA or MCh responses, consistent with possible regulation of these sites by phosphorylation. These results suggest that PMA and MCh both

activate a pathway that can regulate the common PMA-sensitive sites in the I-II linker but that MCh also activates an additional pathway required for regulation of the MCh-unique sites, especially in the II-III linker.

L3 ANSWER 3 OF 25 MEDLINE on STN
AN 2004188880 MEDLINE
DN PubMed ID: 15031612
TI (S,S)-formoterol increases the production of IL-4 in mast cells and the airways of a murine asthma model.
AU Abraha Daniel; Cho Seong H; Agrawal Devendra K; Park Jae M; Oh Chad K
CS Division of Allergy and Immunology, Department of Pediatrics, Harbor-UCLA Medical Center, University of California, Los Angeles, Torrance, CA 90509, USA.
SO International archives of allergy and immunology, (2004 Apr) Vol. 133, No. 4, pp. 380-8. Electronic Publication: 2004-03-17.
Journal code: 9211652. ISSN: 1018-2438.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200405
ED Entered STN: 20040416
Last Updated on STN: 20040511
Entered Medline: 20040510
AB BACKGROUND: Racemic formoterol is an equimolar mixture of (R,R)- and (S,S)-formoterol. Several studies have shown (S,S)-formoterol to have proinflammatory effects. We previously reported that (S)-albuterol increased the secretion of histamine and interleukin (IL)-4 in murine mast cells. We thus hypothesized that (S,S)-formoterol promotes asthma by enhancing IL-4 production in mast cells of the asthmatic airway. METHODS: Murine and human mast cells were stimulated by high affinity IgE receptor (Fc epsilon RI) cross-linking or with phorbol myristate **acetate** /calcium ionophore A23187 (PMA/A23187). Jurkat T cells were stimulated with PMA. Cells were pretreated with either (R,R)- or (S,S)-formoterol. Ovalbumin (OVA)-sensitized BALB/c mice were pretreated with (R,R)- or (S,S)-formoterol before each intranasal OVA challenge for 10 days. Bronchoalveolar lavage fluid was obtained from the mice. The levels of IL-4, histamine and PGD(2) were measured. Early and late allergic responses (EAR and LAR, respectively) to OVA challenge and airway hyperresponsiveness (AHR) were measured. RESULTS: (S,S)-formoterol enhanced the production of IL-4, histamine, and PGD(2) in mast cells, whereas (R,R)-formoterol had no effect. Neither (S,S)- nor (R,R)-formoterol had effect on IL-4 production in Jurkat T cells. In OVA-challenged mice, (S,S)-formoterol increased IL-4 secretion, whereas (R,R)-formoterol had no effect. Finally, (S,S)-formoterol enhanced the inflammatory changes in the peribronchial and perivascular areas without affecting EAR, LAR or AHR, whereas (R,R)-formoterol reduced EAR, LAR and AHR as well as cellular infiltration in the lung tissue of these mice. CONCLUSION: (S,S)-formoterol may exert adverse effects in asthma control by activating mast cells to produce proinflammatory mediators such as IL-4.

L3 ANSWER 4 OF 25 MEDLINE on STN
AN 2004118942 MEDLINE
DN PubMed ID: 15010730
TI Different profile of interleukin-10 production in circulating T cells from atopic asthmatics compared with healthy subjects.
AU Matsumoto K; Narita S; Rerecich T; Snider D P; O'Byrne P M
CS Asthma Research Group, Firestone Institute of Respiratory Health, St Joseph's Healthcare, McMaster University, Hamilton, Ontario.
SO Canadian respiratory journal : journal of the Canadian Thoracic Society, (2004 Jan-Feb) Vol. 11, No. 1, pp. 33-8.
Journal code: 9433332. ISSN: 1198-2241.
CY Canada

DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200408
ED Entered STN: 20040311
Last Updated on STN: 20040810
Entered Medline: 20040809
AB BACKGROUND: Interleukin (IL)-10 is a pleiotropic cytokine released from various cells, including T cells. Although IL-10 is suggested to inhibit allergic responses, its role in asthma remains uncertain. The purpose of the present study was to compare the profile of IL-10 in circulating T cells from stable atopic asthmatics, atopic nonasthmatics and healthy controls. METHODS: Peripheral blood mononuclear cells were isolated, stained with anti-CD3 and CD4/CD8 antibodies, and then processed for intracellular IL-10 detection by flow cytometry. RESULTS: A kinetic study in healthy controls showed that stimulation with phorbol 12-myristate 13-**acetate** and ionomycin significantly increased the frequencies of IL-10-producing CD3+, CD4+ and CD8+ cells. Without stimulation, the frequencies of IL-10-producing CD3+, CD4+ and CD8+cells were significantly higher in asthmatics than in healthy controls, while a similar trend was observed in atopic nonasthmatics. Stimulation for 24 h significantly increased IL-10-producing CD3+, CD4+ and CD8+cells in healthy controls and atopic nonasthmatics, but not in asthmatics. CONCLUSIONS: The frequency of IL-10-producing T cells is increased in the circulation of stable atopic asthmatics compared with normal controls. The lack of enhancement in their frequency by phorbol 12-myristate 13-**acetate** and ionomycin in asthmatics suggests that the circulating T cells of asthmatic subjects are maximally stimulated with regards to IL-10 production; alternatively, IL-10 production by T cells from asthmatics may be regulated differently than T cells from other subjects.

L3 ANSWER 5 OF 25 MEDLINE on STN
AN 2004092154 MEDLINE
DN PubMed ID: 14625305
TI Identification of sites responsible for potentiation of type 2.3 calcium currents by acetyl-beta-methylcholine.
AU Kamatchi Ganesan L; Franke Ruthie; Lynch Carl 3rd; Sando Julianne J
CS Department of Anesthesiology, University of Virginia Health Sciences Systems, Charlottesville, Virginia 22908-0710, USA.. gk3p@virginia.edu
NC GM31184 (NIGMS)
GM65214 (NIGMS)
SO The Journal of biological chemistry, (2004 Feb 6) Vol. 279, No. 6, pp. 4102-9. Electronic Publication: 2003-11-18.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200404
ED Entered STN: 20040302
Last Updated on STN: 20040402
Entered Medline: 20040401
AB To address mechanisms for the differential sensitivity of voltage-gated Ca2+ channels (Cav) to agonists, channel activity was compared in Xenopus oocytes coexpressing muscarinic M(1) receptors and different Cav alpha1 subunits, all with beta1B,alpha2/delta subunits. Acetyl-beta-methylcholine (MCh) decreased Cav 1.2c currents, did not affect 2.1 or 2.2 currents, but potentiated Cav 2.3 currents. Phorbol 12-myristate 13-**acetate** (PMA) did not affect Cav 1.2c or 2.1 currents but potentiated 2.2 and 2.3 currents. Comparison of the amino acid sequences of the alpha1 subunits revealed a set of potential protein kinase C phosphorylation sites in common between the 2.2 and 2.3 channels that respond to PMA and a set of potential sites unique to the alpha1 2.3

subunits that respond to MCh. Quadruple Ser --> Ala mutation of the predicted MCh sites in the alpha1 2.3 subunit (Ser-888, Ser-892, and Ser-894 in the II-III linker and Ser-1987 in the C terminus) caused loss of the MCh response but not the PMA response. Triple Ser --> Ala mutation of just the II-III linker sites gave similar results. Ser-888 or Ser-892 was sufficient for the MCh responsiveness, whereas Ser-894 required the presence of Ser-1987. Ser --> Asp substitution of Ser-888, Ser-892, Ser-1987, and Ser-892/Ser-1987 increased the basal current and decreased the MCh response but did not alter the PMA response. These results reveal that sites unique to the II-III linker of alpha1 2.3 subunits mediate the responsiveness of Cav 2.3 channels to MCh. Because Cav 2.3 channels contribute to action potential-induced Ca2+ influx, these sites may account for M1 receptor-mediated regulation of neurotransmission at some synapses.

L3 ANSWER 6 OF 25 MEDLINE on STN
AN 2003248397 MEDLINE
DN PubMed ID: 12770520
TI Cholinergic responses of seminal vesicles isolated from rats exposed perinatally to hydrocortisone.
AU Pereira O C M; Yasuhara F; Arena A C
CS Department of Pharmacology, Institute of Biosciences-Sao Paulo State University (UNESP), Botucatu, 18 618-000, Sao Paulo, Brazil.. pereira@ibb.unesp.br
SO Pharmacological research : the official journal of the Italian Pharmacological Society, (2003 Jul) Vol. 48, No. 1, pp. 91-5. Journal code: 8907422. ISSN: 1043-6618.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200407
ED Entered STN: 20030529
Last Updated on STN: 20031217
Entered Medline: 20040709
AB This study was performed in order to investigate the cholinomimetic response of seminal vesicles isolated from rats treated with hydrocortisone **acetate** during perinatal life. At the adult phase, the body weight and the wet weight of the seminal vesicle of these animals were unchanged. However, these male rats exhibited a significant reduction in plasma testosterone concentration. A significant increase in the sensitivity of the seminal vesicle to acetylcholine was also observed. Despite this, there was a significant reduction in the maximum contractile response of the organ to this transmitter. These results indicate that exposure to hydrocortisone during the critical period of brain sexual differentiation has a long-term effect on testosterone production of male rats. In addition, physiological levels of cortisone in perinatal life are also essential to support the contractile response pattern of the seminal vesicle to acetylcholine in adult life, probably crucial to the reproductive process.

L3 ANSWER 7 OF 25 MEDLINE on STN
AN 2003215700 MEDLINE
DN PubMed ID: 12663092
TI Distinct regulation of expressed calcium channels 2.3 in Xenopus oocytes by direct or indirect activation of protein kinase C.
AU Kamatchi Ganesan L; Tiwari Shveta N; Chan Carrie K; Chen Daguang; Do Sang-Hwan; Durieux Marcel E; Lynch Carl 3rd
CS Department of Anesthesiology, P.O. Box 800710, University of Virginia Health Sciences Systems, Charlottesville, VA 22908-0710, USA.. gk3p@virginia.edu
NC GM31144 (NIGMS)
R29-GM52387 (NIGMS)
SO Brain research, (2003 Apr 11) Vol. 968, No. 2, pp. 227-37. Journal code: 0045503. ISSN: 0006-8993.

CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200307
ED Entered STN: 20030513
Last Updated on STN: 20030708
Entered Medline: 20030707
AB Protein kinase C (PKC)-dependent regulation of voltage-gated Ca (Ca(v); with alpha(1)beta1Balpha2/delta subunits) channel 2.3 was investigated using phorbol 12-myristate 13-**acetate** (PMA), or by M(1) muscarinic receptor activation in Xenopus oocytes. The inward Ca(2+)-current with Ba(2+) (I(Ba)) as the charge carrier was potentiated by PMA or acetyl-beta-methylcholine (MCh). The inactivating [I(inact)] and non-inactivating [I(noninact)] components of I(Ba) and the time constant of inactivation tau(inact) were all increased by MCh or PMA. This may be a PKC-dependent action since the effect of MCh and PMA was blocked by Ro-31-8425 or beta-pseudosubstrate. MCh effect was blocked by atropine, guanosine-5'-O-(2-thiodiphosphate) trilithium (GDPbetaS) or U-73122. The effect of MCh but not PMA was blocked by the inhibition of inositol-1,4,5-trisphosphate (IP3) receptors, intracellular Ca(2+) ([Ca(2+)](i)) or the translocation of conventional PKC (cPKC) with heparin, BAPTA and betaC2.4, respectively. While a lower concentration (25 nM) of Ro-31-8425 blocked MCh, a higher concentration (500 nM) of Ro-31-8425 was required to block PMA action. This differential susceptibility of MCh and PMA to heparin, BAPTA, betaC2.4 or Ro-31-8425 is suggestive of the involvement of Ca(2+)-dependent cPKC in MCh action, whereas cPKC and Ca(2+)-independent novel PKC (nPKC) in PMA action. PMA led to additional increase in I(Ba) that was already potentiated by preadministered MCh (1 or 10 microM), leading to the suggestion that differential phosphorylation sites for cPKC and nPKC may be present in the alpha(1)2.3 subunit of Ca(v) 2.3 channels.

L3 ANSWER 8 OF 25 MEDLINE on STN
AN 2003076974 MEDLINE
DN PubMed ID: 12587288
TI Inflammatory effects of inhaled endotoxin-contaminated metal working fluid aerosols in rats.
AU DeLorme Michael P; Gao Xiufeng; Doyon-Reale Nicole; Barraclough-Mitchell Holly; Bassett David J P
CS Department of Occupational and Environmental Health Sciences, Wayne State University, Detroit, Michigan, USA.. michael.p.delorme@usa.dupont.com
NC R01 HL34674 (NHLBI)
SO Journal of toxicology and environmental health. Part A, (2003 Jan 10) Vol. 66, No. 1, pp. 7-24.
Journal code: 100960995. ISSN: 1528-7394.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200303
ED Entered STN: 20030218
Last Updated on STN: 20030314
Entered Medline: 20030313
AB Exposure to aerosols generated from water-soluble metal-working fluids (MWF) is associated with numerous respiratory symptoms consistent with an acute pulmonary inflammatory event. Previous studies in mice and guinea pigs have implicated endotoxin contamination of MWF as the causative agent responsible for inducing pulmonary neutrophilia and decrements in airway conductance. However, little information is known about the relationship between endotoxin-contaminated MWF exposure and changes in airway physiology. The present study, utilizing a rat model, has demonstrated that exposure to 10 mg/m3 with endotoxin (0 to 3.2 micrograms/m3) resulted in a time- and concentration-dependent migration of neutrophils in the lung tissue's interstitial spaces as well as the lavageable airways. In

contrast to other airborne toxicants, where neutrophil infiltration of the lung has been associated with hyperresponsive airways, the endotoxin-induced neutrophilia observed in the present study was not associated with airway hyperresponsiveness to challenge with the muscarinic agent methacholine or with permeability damage to the lung. Bronchoalveolar lavage (BAL)-recovered neutrophils demonstrated no adverse effects as a result of endotoxin-contaminated MWF exposure. In contrast, a population of alveolar macrophages was observed to be enlarged in size and demonstrated an increased sensitivity to oxidative metabolism when challenged with phorbol myristate **acetate**, consistent with being at a relatively high state of activation. These results suggest that while endotoxin contamination of MWF is capable of producing an acute inflammatory event, other predisposition factors may be required to induce alterations in pulmonary physiology.

L3 ANSWER 9 OF 25 MEDLINE on STN
AN 2002638157 MEDLINE
DN PubMed ID: 12396876
TI Hyperresponsive airways correlate with lung tissue inflammatory cell changes in ozone-exposed rats.
AU DeLorme Michael P; Yang Hui; Elbon-Copp Constance; Gao Xiufeng; Barraclough-Mitchell Holly; Bassett David J P
CS Department of Occupational and Environmental Health Sciences, Wayne State University, Detroit, Michigan, USA.. michael.p.delorme@usa.dupont.com
NC R01 HL34674 (NHLBI)
SO Journal of toxicology and environmental health. Part A, (2002 Oct 11) Vol. 65, No. 19, pp. 1453-70.
Journal code: 100960995. ISSN: 1528-7394.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200211
ED Entered STN: 20021026
Last Updated on STN: 20021211
Entered Medline: 20021107
AB The role of inflammatory cell infiltration in the development of hyperresponsiveness of the airways to muscarinic challenge remains poorly understood. Unlike previous investigations that only examined conducting airway inflammation, the present study utilized both bronchoalveolar lavage (BAL) and lung tissue digestion to determine rat lung inflammatory cell contents following a 4-h exposure to 2 ppm ozone. Immediately following ozone exposure, neutrophil content of the lung tissue was significantly increased and reached a value that was fourfold higher than air-exposed controls by 3 h postexposure. Although lavage-recovered neutrophils were elevated at 24 h, tissue neutrophil numbers had returned to control values. This transient elevation of tissue neutrophils directly correlated with an elevation and subsequent decline of airway hyperresponsiveness, measured as a decrease in the intravenous dose of methacholine provoking a 200% increase in airway resistance (PD(200)R). Animals rendered neutropenic with a rabbit anti-rat neutrophil serum prior to exposure were protected from ozone-induced hyperresponsive airways, further demonstrating an association between neutrophil infiltration into the lung and altered airway physiology. Although BAL-recovered neutrophils demonstrated no adverse effects as a result of ozone exposure, macrophages were not only found to be necrotic but also displayed altered oxidative metabolism when challenged with phorbol myristate **acetate**. Thus, changes in the microenvironment of the airways smooth muscle were shown to be associated with transient accumulation of neutrophils within the lung tissue and abnormalities of bronchoalveolar lavage-recovered macrophages.

L3 ANSWER 10 OF 25 MEDLINE on STN
AN 2001427067 MEDLINE
DN PubMed ID: 11473864

TI The effects of isoflurane on native and chimeric muscarinic acetylcholine receptors: the role of protein kinase C.
AU Do S H; Kamatchi G L; Durieux M E
CS Department of Anesthesiology, University of Virginia Health Sciences Center, Charlottesville, VA 22908-0710, USA..
sd4z@hscmail.mcc.virginia.edu
SO Anesthesia and analgesia, (2001 Aug) Vol. 93, No. 2, pp. 375-81 , 3rd contents page.
Journal code: 1310650. ISSN: 0003-2999.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200108
ED Entered STN: 20010820
Last Updated on STN: 20010820
Entered Medline: 20010816
AB By using two electrode voltage clamps, we investigated the effects of isoflurane on m3 and chimeric m1/m3 muscarinic receptors and the role of protein kinase C (PKC) in the effects. Muscarinic receptors were expressed by injection of mRNA into Xenopus oocytes, and Ca(2+)-activated Cl(-) currents were measured after the application of acetyl-beta-methylcholine. We constructed chimeric m1/m3 receptor DNA encoding the third intracellular loop of m1 and the remainder from the m3 receptor. Chimeric and m3 receptors were inhibited by isoflurane, but the m1 receptor was not. PKC activation with phorbol-12-myrisate-13-**acetate** (50 nM) decreased signaling of both chimeric and m3 receptors significantly. Chelerythrine (20 microM, PKC inhibitor) abolished the effect of isoflurane on chimeric and m3 signaling. Whereas isoflurane inhibition of chimeric and m3 receptors was completely reversible after washout with Tyrode's solution for 3 min, treatment with okadaic acid (500 nM, protein phosphatase inhibitor) rendered the inhibition irreversible. Taken together, our results suggest that isoflurane inhibits m3 and chimeric m1/m3 muscarinic signaling by enhancing PKC activity and that the site of action is located outside of the third intracellular loop. IMPLICATIONS: By use of the Xenopus oocyte expression system, we investigated the effects of isoflurane on muscarinic signaling and the role of protein kinase C in these effects. Our findings suggest that isoflurane inhibits muscarinic receptors through activation of protein kinase C and that the relevant phosphorylation sites are located outside the third intracellular loop.

L3 ANSWER 11 OF 25 MEDLINE on STN
AN 2000451442 MEDLINE
DN PubMed ID: 11007130
TI Effects of elevated cytoplasmic calcium and protein kinase C on endoplasmic reticulum structure and function in HEK293 cells.
AU Pedrosa Ribeiro C M; McKay R R; Hosoki E; Bird G S; Putney J W Jr
CS National Institute of Environmental Health Sciences, National Institute of Health, Research Triangle Park, North Carolina 27709, USA.
SO Cell calcium, (2000 Mar) Vol. 27, No. 3, pp. 175-85.
Journal code: 8006226. ISSN: 0143-4160.
CY SCOTLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200101
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010104
AB In human embryonic kidney (HEK) cells stably transfected with green fluorescent protein targeted to the endoplasmic reticulum (ER), elevation of intracellular Ca2+ ([Ca2+]i) altered ER morphology, making it appear punctate. Electron microscopy revealed that these punctate structures represented circular and branched rearrangements of the endoplasmic

reticulum, but did not involve obvious swelling or pathological fragmentation. Activation of protein kinase C with phorbol 12-myristate 13-**acetate** (PMA), prevented the effects of ionomycin on ER structure without affecting the elevation of [Ca2+]i. These results suggest that protein kinase C activation alters cytoplasmic or ER components underlying the effects of high [Ca2+]i on ER structure. Treatment of HEK cells with PMA also reduced the size of the thapsigargin-sensitive Ca2+ pool and inhibited Ca2+ entry in response to thapsigargin. Thus, protein kinase C activation has multiple actions on the calcium storage and signalling function of the endoplasmic reticulum in HEK cells: (1) reduced intracellular Ca2+ storage capacity, (2) inhibition of capacitative Ca2+ entry, and (3) protection of the endoplasmic reticulum against the effects of high [Ca2+]i.

L3 ANSWER 12 OF 25 MEDLINE on STN
AN 2000237739 MEDLINE
DN PubMed ID: 10773003
TI Effects of volatile anesthetics on the direct and indirect protein kinase C-mediated enhancement of alpha1E-type Ca(2+) current in Xenopus oocytes.
AU Kamatchi G L; Tiwari S N; Durieux M E; Lynch C 3rd
CS Department of Anesthesiology, University of Virginia Health Science System, Charlottesville, Virginia 22908-0710, USA.. gk3p@virginia.edu
NC GM31144 (NIGMS)
R29-GM52387 (NIGMS)
SO The Journal of pharmacology and experimental therapeutics, (2000 May) Vol. 293, No. 2, pp. 360-9.
Journal code: 0376362. ISSN: 0022-3565.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200006
ED Entered STN: 20000629
Last Updated on STN: 20000629
Entered Medline: 20000621
AB The effect of the volatile anesthetics (VAs) halothane (0.59 mM) and isoflurane (0.70 mM) on protein kinase C (PKC)-mediated modulation of alpha1E type of high-voltage-gated Ca(2+) channels was examined in Xenopus oocytes coexpressing m1 muscarinic acetylcholine receptors. Phorbol-12-myristate-13-**acetate** (PMA) or 1, 2-dioctanoyl-sn-glycerol (DOG) was used to activate PKC directly, whereas indirect activation was induced with acetyl-beta-methylcholine (MCh). The interaction between PKC activators and VAs was examined by perfusing either VA before, during, or after the administration of PMA, DOG, or MCh. In addition, the effect of VAs was studied after the down-regulation of PKC. The application of VAs inhibited Ba(2+) current (I(Ba)), whereas PMA (500 nM), DOG (100 microM), or MCh (1 and 10 microM) markedly potentiated I(Ba). VAs inhibited PMA- or DOG-enhanced I(Ba) to the same extent as seen in controls. The inhibition of I(Ba) induced by VAs was not reversed by PMA or DOG. The administration of VAs in combination with PMA, DOG, or MCh (1 microM) led to the inhibition of I(Ba). MCh (10 microM) counteracted the inhibitory effect of VAs when administered together and reversed the inhibition of I(Ba) produced by VAs. These differences in the responses between PMA and MCh (10 microM) may be based on the involvement of various pools of PKC. It is suggested that VAs act directly at the membrane, because they blocked the membrane-based action of PMA, whereas the receptor-based action of MCh was only partially blocked. It is possible that some PKC isoforms may not be a direct target of VAs.

L3 ANSWER 13 OF 25 MEDLINE on STN
AN 1998302161 MEDLINE
DN PubMed ID: 9638314
TI Synergistic effects of ularitide **acetate** with classical bronchorelaxants on guinea-pig tracheal smooth muscle.

AU Korn C; Neidlein R; Strein K; Wilhelms O H
CS Pharmaceutical-Chemical Institute, University of Heidelberg, Germany.
SO Arzneimittel-Forschung, (1998 May) Vol. 48, No. 5, pp. 475-81.
Journal code: 0372660. ISSN: 0004-4172.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199807
ED Entered STN: 19980723
Last Updated on STN: 19990129
Entered Medline: 19980716
AB Ularitide (CAS 118812-69-4, urodilatin) is a member of the family of the atrial natriuretic peptides. In the present study, the relaxant effects of ularitide **acetate**, isoproterenol (isoprenaline) hemisulfate, aminophylline, zaprinast, and different combinations between these drugs were investigated on **methacholine chloride** -precontracted guinea-pig tracheal smooth muscle. Ularitide **acetate** was a weaker bronchorelaxant than isoproterenol hemisulfate and aminophylline. Moreover the relaxation induced by ularitide **acetate** was reversible, while the relaxation induced by isoproterenol hemisulfate, aminophylline, and zaprinast was irreversible. Combinations between in each case two of these substances were overadditive, if the phosphodiesterase-inhibiting component was applicated before the combination partner. Their effects were only additive, if the combination partners were applicated simultaneously. All combinations between ularitide **acetate** and isoproterenol hemisulfate, aminophylline, or zaprinast respectively relaxed the tracheas irreversibly. These results suggest that ularitide **acetate** might be a novel partner for classical bronchorelaxants in potent bronchorelaxing combinations in the therapy of asthma bronchiale.

L3 ANSWER 14 OF 25 MEDLINE on STN
AN 97393043 MEDLINE
DN PubMed ID: 9249560
TI Na-K-2Cl cotransporters are present and regulated in simian eccrine clear cells.
AU Toyomoto T; Knutsen D; Soos G; Sato K
CS Marshall Dermatology Research Laboratories, Department of Dermatology, University of Iowa College of Medicine, Iowa City 52242, USA.
NC AR-25339 (NIAMS)
DK-27857 (NIDDK)
SO The American journal of physiology, (1997 Jul) Vol. 273, No. 1 Pt 2, pp. R270-7.
Journal code: 0370511. ISSN: 0002-9513.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199709
ED Entered STN: 19970916
Last Updated on STN: 19990129
Entered Medline: 19970903
AB In freshly dissociated rhesus palm eccrine clear cells, regulatory volume increase (RVI) was studied using image analysis as a measure of Na-K-2Cl cotransport activity. Pseudo-RVIs, as well as RVI during methacholine (MCh)-induced cell shrinkage, were observed in clear cells and were inhibited by 100 microM bumetanide or in Na-free medium, but were not inhibited by amiloride or ouabain. RVI in hypertonic medium and RVI after MCh-induced cell shrinkage were accelerated by adenosine 3',5'-cyclic monophosphate (cAMP)-elevating agents (forskolin+isoproterenol) and inhibited by phorbol ester. RVI in hypertonic medium was enhanced by a phosphatase inhibitor, okadaic acid. mRNA for Na-K-2Cl cotransporter (NaKCC) was demonstrated in freshly isolated rhesus sweat secretory coils by polymerase chain reaction (PCR) after reverse transcription using a set

of primers derived from the published human NaKCC (hNaKCC) 1 sequence, i.e., nucleotides 2,043-2,810. The deduced amino acid sequence of the PCR-amplified 767-base pair segment was identical to that of hNaKCC 1 from a human colon cell line (T84). The data are interpreted to indicate that NaKCC, showing strong homology to secretory type hNaKCC 1, is present in rhesus eccrine secretory coils and may participate in the cotransport component of eccrine sweat secretion and cell volume regulation, especially during cholinergic stimulation. The data also raise the possibility that sweat gland NaKCC may be upregulated by cAMP-mediated protein phosphorylation and downregulated by protein kinase C.

L3 ANSWER 15 OF 25 MEDLINE on STN
AN 95212677 MEDLINE
DN PubMed ID: 7698439
TI Phospholipase D does not mediate alcohol inhibition of [3H]-noradrenaline release from SH-SY5Y cells.
AU Purkiss J R
CS Department of Cell Physiology and Pharmacology, University of Leicester, U.K.
SO Biochemical Society transactions, (1994 Nov) Vol. 22, No. 4, pp. 419S.
Journal code: 7506897. ISSN: 0300-5127.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199505
ED Entered STN: 19950510
Last Updated on STN: 19990129
Entered Medline: 19950504

L3 ANSWER 16 OF 25 MEDLINE on STN
AN 95046225 MEDLINE
DN PubMed ID: 7957828
TI Increased PMA-induced chemiluminescence from whole blood of patients with bronchial hyperreactivity.
AU Nordman S; Nyberg P; Linko L
CS Mjolbolsta Hospital, Finland.
SO The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology, (1994 Aug) Vol. 7, No. 8, pp. 1425-30.
Journal code: 8803460. ISSN: 0903-1936.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199412
ED Entered STN: 19950110
Last Updated on STN: 19990129
Entered Medline: 19941221
AB Blood phagocytes from patients with asthma have an increased capacity to produce reactive oxygen metabolites. We studied whether whole blood luminol-dependent chemiluminescence could detect this phenomenon in patients with a normal spirometry but bronchial hyperreactivity as determined with a methacholine bronchial challenge test. Whole blood chemiluminescence, serum eosinophilic cationic protein (ECP), and serum myeloperoxidase (MPO) were determined from 50 patients referred for a methacholine challenge due to prolonged cough and/or dyspnoea. The chemiluminescence results were compared to those from 15 healthy persons. The hyperreactive patients (n = 18) had significantly higher phorbol 12-myristate 13-acetate (PMA)-induced whole blood chemiluminescence values (mean 18.8 mV.min-1; 95% confidence limits (C.L.) 16.3-21.3 mV.min-1) than the normoreactive patients (mean 14.2 mV.min-1; 95% C.L. 13.0-15.5 mV.min-1;) and the healthy controls (mean 12.8 mV.min-1; 95% C.L. 11.7-13.9 mV.min-1). There was no significant difference in PMA-induced chemiluminescence between the normoreactive

patients and the controls. The hyperreactive patients had higher serum ECP values than the normoreactive patients, but there was no correlation between whole blood chemiluminescence and serum ECP levels or total eosinophil count. There was no significant difference in monocyte reactive oxygen metabolite production or serum MPO values between the normoreactive and the hyperreactive patients. We suggest that the increased PMA-induced whole blood chemiluminescence in bronchial hyperreactivity is due mainly to an activation of neutrophils, and that the assay might be useful as a systemic inflammatory marker in patients with pulmonary inflammatory processes resulting in bronchial hyperreactivity.

L3 ANSWER 17 OF 25 MEDLINE on STN
AN 94166414 MEDLINE
DN PubMed ID: 7509909
TI NG-monomethyl-L-ARG reduces the forearm vasodilator response to acetylcholine but not to methacholine in humans.
AU Rongen G A; Smits P; Thien T
CS Department of Medicine, University Hospital Nijmegen, The Netherlands.
SO Journal of cardiovascular pharmacology, (1993 Dec) Vol. 22, No. 6, pp. 884-8.
Journal code: 7902492. ISSN: 0160-2446.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199404
ED Entered STN: 19940412
Last Updated on STN: 19990129
Entered Medline: 19940405
AB We compared the contribution of nitric oxide (NO) in methacholine (MCh)- and acetylcholine (ACh)-induced vasodilation using the NO-synthase inhibitor NG-monomethyl-L-arginine **acetate** (L-NMMA-**acetate**) in two groups (A and B) of 6 healthy male volunteers. The left brachial artery was cannulated for drug infusion and recording of mean arterial pressure (MAP). Forearm blood flow (FBF) was measured on both sides by venous occlusion mercury-in-silastic strain-gauge plethysmography. All measurements were performed with occluded hand circulation. Forearm vasodilator response to three increasing dosages of MCh (0.03, 0.3, and 1 micrograms/100 ml forearm/min; group A) or ACh (0.5, 2, and 8 micrograms/100 ml forearm/min; group B) was studied first. Forty-five minutes later, these infusions were repeated (after and during local administration of L-NMMA). L-NMMA-**acetate** infusion alone increased basal forearm vascular resistance (FVR, mean +/- SE) by 86.2 +/- 14.5 and 99.5 +/- 27.4% in groups A and B, respectively ($p < 0.05$) without significant FVR changes in the control arm. MCh-induced vasodilation was not attenuated by concomitant L-NMMA-**acetate** infusion. In contrast, L-NMMA-**acetate** significantly reduced the averaged percentage decrease in FVR during infusion of ACh from 55.7 +/- 9.1 to 35.4 +/- 11.8% ($p < 0.05$). L-NMMA-**acetate** increased basal vascular tone and reduced the vasodilator response to ACh. MCh induced vasodilation to a degree similar to that obtained with ACh. Nevertheless, MCh-induced vasodilation could not be attenuated by L-NMMA, suggesting that NO contributes differentially to methacholine- and ACh-induced vasodilation in humans.

L3 ANSWER 18 OF 25 MEDLINE on STN
AN 94023508 MEDLINE
DN PubMed ID: 8210761
TI A stimulatory role of protein kinase C in feline tracheal submucosal gland secretion.
AU Shimura S; Ishihara H; Nagaki M; Sasaki H; Takishima T
CS First Department of Internal Medicine, Tohoku University School of Medicine, Sendai, Japan.
SO Respiration physiology, (1993 Aug) Vol. 93, No. 2, pp. 239-47.

Journal code: 0047142. ISSN: 0034-5687.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199311
ED Entered STN: 19940117
Last Updated on STN: 19990129
Entered Medline: 19931108
AB To determine the role of protein kinase C (PKC) in airway submucosal gland secretion, we examined the effect of a selective PKC stimulant, phorbol 12-myristate 13-**acetate** (PMA), on mucus glycoprotein (MGP) secretion, fluid secretion and intracellular Ca2+ concentration ([Ca2+]i) in isolated feline submucosal glands. MGP and fluid secretions were estimated by measuring trichloroacetic acid (TCA)-precipitable glycoconjugates and 22Na-efflux, respectively, from isolated glands. [Ca2+]i was measured using a Ca(2+)-sensitive fluorescent dye, Fura 2. PMA itself produced a significant increase in MGP secretion in a dose-dependent fashion (173% of control at 10(-5) M). PMA also produced a significant increase in 22Na-efflux (151% of baseline rate constant at 10(-5) M). Indomethacin failed to alter the increase in MGP secretion or in 22Na-efflux in response to PMA. Two PKC inhibitors, 1-(5-isoquinolinesulfonyl)-2-methylpiperazine (H-7) and sphingosine, inhibited both MGP secretion and 22Na-efflux stimulated by PMA; there was only a partial inhibition after stimulation by methacholine (MCh). PMA did not significantly alter [Ca2+]i and H-7 did not alter the MCh-induced [Ca2+]i rise. These findings indicate that PKC has a direct stimulatory role in stimulus-secretion coupling of airway submucosal gland secretion.

L3 ANSWER 19 OF 25 MEDLINE on STN
AN 90182654 MEDLINE
DN PubMed ID: 2138056
TI Calcium efflux across the plasma membrane of rat parotid acinar cells is unaffected by receptor activation or by the microsomal calcium ATPase inhibitor, thapsigargin.
AU Takemura H; Thastrup O; Putney J W Jr
CS Calcium Regulation Section, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, North Carolina.
SO Cell calcium, (1990 Jan) Vol. 11, No. 1, pp. 11-7.
Journal code: 8006226. ISSN: 0143-4160.
CY SCOTLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199004
ED Entered STN: 19900601
Last Updated on STN: 19990129
Entered Medline: 19900419
AB The rate of Ca2+ extrusion across the plasma membrane of rat parotid acinar cells was determined by measuring the decay of the intracellular calcium concentration, [Ca2+]i, following the addition of EGTA to agonist stimulated cells. In the presence of extracellular Ca2+, the muscarinic cholinergic receptor agonist, methacholine, rapidly increased [Ca2+]i (peaking within 5 s), which then decreased to a higher steady state level. This elevated steady state level was dependent on extracellular Ca2+ concentration. Likewise, thapsigargin, a non-phorbol ester tumor promoter that does not increase inositol phosphates, gradually increased [Ca2+]i, peaking within 1 min and then declining to a new elevated plateau level which was also dependent on extracellular Ca2+. [Ca2+]i, elevated by methacholine or thapsigargin, was rapidly decreased by the addition of EGTA by a process the kinetics of which depended on the value of [Ca2+]i before the addition of EGTA. That is, [Ca2+]i increased as a function of the extracellular Ca2+ concentration and also the apparent half-time for Ca2+ extrusion following the addition of EGTA to cells was increased as

the [Ca2+]i increased. This presumably reflects the saturable nature of the Ca2+ extrusion mechanism. The steady state [Ca2+]i in cells stimulated with methacholine or thapsigargin in nominally Ca2+ free medium was similar to the steady state [Ca2+]i in unstimulated cells in normal, Ca2(+)-containing medium. Under these similar [Ca2+]i conditions, stimulated and unstimulated cells showed a similar time course of decay upon addition of EGTA. In addition, neither methacholine nor phorbol myristate **acetate** decreased the sustained elevation of [Ca2+]i induced by ionomycin.(ABSTRACT TRUNCATED AT 250 WORDS)

L3 ANSWER 20 OF 25 MEDLINE on STN
AN 89234979 MEDLINE
DN PubMed ID: 2541190
TI Superoxide generation and its modulation by adenosine in the neutrophils of subjects with asthma.
AU Meltzer S; Goldberg B; Lad P; Easton J
CS Department of Allergy and Clinical Immunology, Kaiser Permanente Medical Center, Los Angeles, Calif 90027.
NC AM30878 (NIADDK)
AM34550 (NIADDK)
SO The Journal of allergy and clinical immunology, (1989 May) Vol. 83, No. 5, pp. 960-6.
Journal code: 1275002. ISSN: 0091-6749.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198906
ED Entered STN: 19900306
Last Updated on STN: 19990129
Entered Medline: 19890615
AB Airway inflammation with neutrophil infiltration may play a role in airway hyperreactivity. Neutrophils may exert their effects through the generation of superoxide O2- anion and other oxygen-derived free radicals. O2- generation by neutrophils has been demonstrated to be modulated by adenosine at physiologic concentrations. Therefore, we have investigated the function of peripheral blood neutrophils with respect to O2- anion generation and its regulation by adenosine in both subjects with asthma and normal subjects and also the relationship between O2- anion generation and airway hyperresponsiveness in subjects with asthma. Purified neutrophils were obtained from eight subjects with stable asthma and seven normal control subjects not taking chronic medications. O2- anion generation in subjects with asthma was significantly higher compared with that of normal subjects after stimulation with either N-formyl-methionyl-leucyl-phenylalanine (mean, 14.8 nmol/10(6) cells for subjects with asthma versus mean, 9.6 nmol/10(6) cells for normal subjects; p less than 0.01) or phorbol myristate **acetate** (mean, 13.6 nmol/10(6) cells versus mean, 8.1 nmol/10(6) cells; p less than 0.05). Adenosine inhibited N-formyl-methionyl-leucyl-phenylalanine-stimulated O2- anion generation in a dose-related fashion in subjects with asthma and normal subjects to a similar degree. Adenosine had no effect on O2- anion generation after phorbol myristate **acetate** stimulation. These results indicate that neutrophils from subjects with asthma produce more O2- anion when they are stimulated than do neutrophils from normal subjects and that this difference is not due to adenosine modulation. In subjects with asthma, O2- anion generation correlated with the degree of airway hyperresponsiveness to inhaled methacholine.

L3 ANSWER 21 OF 25 MEDLINE on STN
AN 89066680 MEDLINE
DN PubMed ID: 3058689
TI Ca2+ influx causes rapid translocation of protein kinase C to membranes. Studies of the effects of secretagogues in adrenal chromaffin cells.
AU TerBush D R; Bittner M A; Holz R W
CS Department of Pharmacology, University of Michigan, Ann Arbor 48109-0626.

NC RO 1 DK27959 (NIDDK)
SO The Journal of biological chemistry, (1988 Dec 15) Vol. 263, No. 35, pp. 18873-9.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198901
ED Entered STN: 19900308
Last Updated on STN: 19990129
Entered Medline: 19890120
AB In bovine adrenal chromaffin cells nicotinic stimulation or a depolarizing concentration of K+ caused a rapid, transient translocation to membranes of as much as 14% of the total cellular protein kinase C activity. The quantitative relationship between membrane-bound protein kinase C and Ca2+-dependent secretion was determined in cells rendered leaky by digitonin treatment. Intact cells were incubated with various concentrations of 12-O-tetradecanoylphorbol-13-**acetate** (TPA) to activate and cause translocation of protein kinase C to membrane before permeabilization in the presence of Ca2+. For the same amount of membrane-bound protein kinase C, a similar degree of enhancement of Ca2+-dependent secretion occurred in cells incubated for 1 or 30 min with TPA. Translocation of as little as 2-3% of the cellular protein kinase C to the membrane enhanced Ca2+-dependent secretion by 25-30%. Muscarinic agonists caused a 5% increase in membrane-bound protein kinase C at 2 s which rapidly reversed. Nicotinic and muscarinic receptor-mediated increases in membrane-bound protein kinase C were additive at 10 s and synergistic at 3 min. Muscarinic stimulation enhanced nicotinic receptor-dependent secretion. Prior incubation with TPA caused a similar enhancement of nicotinic-mediated secretion. The data indicate that protein kinase C which is translocated within seconds of stimulation of the cells with a nicotinic agonist or elevated K+ probably enhances the secretory response immediately or soon after exocytosis begins. In addition, the muscarinic receptor-mediated enhancement of nicotinic receptor-stimulated secretion may be due to newly activated protein kinase C.

L3 ANSWER 22 OF 25 MEDLINE on STN
AN 87264547 MEDLINE
DN PubMed ID: 3299876
TI The effect of lead on cholinergic contractile function in the rat forestomach.
AU Ryden E B; Walsh C T
NC HS 02665 (AHCPR)
SO Toxicology, (1987 Jul) Vol. 45, No. 1, pp. 65-78.
Journal code: 0361055. ISSN: 0300-483X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198707
ED Entered STN: 19900305
Last Updated on STN: 19990129
Entered Medline: 19870731
AB Previous studies have demonstrated that subchronic exposure to lead in rats slows gastric emptying. Therefore, the isometric contractile response of the forestomach from lead-treated rats was examined in vitro. Male Wistar rats were fed 4% lead **acetate** in their diet (NIH-07); controls were pair-fed. After 7 weeks, blood lead levels reached 180-389 micrograms/dl. The forestomach was dissected and suspended in buffer which for lead-treated rats contained 1.2 X 10(-5) M lead **acetate**. Subchronic lead exposure had no effect on the maximum tonic contraction induced by KCl, methacholine or serotonin. However, lead-treated tissue showed enhanced sensitivity to methacholine

with a reduction in EC50 to 59.7% of control. This effect was not observed in control tissue exposed to lead (1.2 X 10(-5) M) only in vitro. Higher in vitro concentrations of lead (16 X 10(-5) M) produced an increase in methacholine EC50. Physostigmine-induced increase in tension was also significantly greater in tissue from lead-treated rats. Electric field stimulation, which produced a contraction attributable to postganglionic acetylcholine release, was unaltered in lead-treated tissue. These results indicate that lead intoxication did not impair the contractile apparatus of the forestomach smooth muscle. The lack of net effect on activation of intramural cholinergic neurons, despite the enhanced sensitivity to a cholinergic agonist, may indicate reduction in acetylcholine release in lead-treated tissue.

L3 ANSWER 23 OF 25 MEDLINE on STN
AN 87109477 MEDLINE
DN PubMed ID: 3543028
TI Differentiation-associated decrease in muscarinic receptor sensitivity in human neuroblastoma cells.
AU Heikkila J E; Scott I G; Suominen L A; Akerman K E
SO Journal of cellular physiology, (1987 Jan) Vol. 130, No. 1, pp. 157-62.
Journal code: 0050222. ISSN: 0021-9541.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198703
ED Entered STN: 19900303
Last Updated on STN: 19990129
Entered Medline: 19870311
AB Muscarinic receptor-linked increases in intracellular free Ca2+ as measured with quin-2 and Ca2+ release from monolayers of cells have been measured in the human neuroblastoma cell line SH-SY5Y. Induction of differentiation with the phorbol ester 12-O-tetradecanoylphorbol-13-**acetate** (TPA) leads to a decrease in the sensitivity of the cells to low concentrations of agonists with respect to the induced increase in cytosolic free Ca2+ and stimulation of Ca2+ efflux. No decrease in agonist binding affinity was observed when the displacement of a labelled antagonist, 3H-NMS, by a non-labelled agonist was studied.

L3 ANSWER 24 OF 25 MEDLINE on STN
AN 86157145 MEDLINE
DN PubMed ID: 2420243
TI Increased metachromatic cells and lymphocytes in bronchoalveolar lavage fluid of dogs with airway hyperreactivity.
AU Hirshman C A; Austin D R; Klein W; Hanifin J M; Hulbert W
NC RO1 HL-25831 (NHLBI)
SO The American review of respiratory disease, (1986 Mar) Vol. 133, No. 3, pp. 482-7.
Journal code: 0370523. ISSN: 0003-0805.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198604
ED Entered STN: 19900321
Last Updated on STN: 19990129
Entered Medline: 19860409
AB Bronchoalveolar lavage (BAL) was performed in 11 basenji greyhound (BG) dogs, which showed persistent airway hyperreactivity to methacholine and citric acid aerosols, and in 15 non-BG dogs, which were significantly less reactive to these challenges. Five of the BG dogs had never received any aerosols prior to BAL, and 3 of the non-BG dogs were allergic to Ascaris suum. No dog received aerosols for 2 wk prior to BAL. Fluid recovered was centrifuged, and aliquots were taken for histamine content and cell identification. Total cell numbers were similar in BG and non-BG dogs.

The BG dogs had increased percentages of lymphocytes and metachromatic cells in BAL fluid compared with those in non-BG dogs. Lymphocytes averaged 35.5 +/- 2.3% (mean +/- SEM) and 17.2 +/- 1.2% (p less than 0.005) in BG and non-BG dogs, respectively. The BG dogs that had received previous aerosol challenge and the BG dogs never challenged had 6.2 +/- 0.4% (mean +/- SEM) and 4.6 +/- 0.6% metachromatic cells in BAL. Nonallergic non-BG dogs had 0.91 +/- 0.2% and allergic non-BG dogs had 2.6 +/- 0.5% metachromatic cells in BAL (p less than 0.05 from BG). Total histamine closely correlated with numbers of metachromatic cells in BAL (r = 0.86). Forty-nine percent fewer mast cells were detected in cell preparations fixed in formalin than in cell preparations fixed in basic lead acetate. Electron micrographs revealed 2 mast cell types on the basis of structural characteristics of the granules.(ABSTRACT TRUNCATED AT 250 WORDS)

L3 ANSWER 25 OF 25 MEDLINE on STN
AN 83114938 MEDLINE
DN PubMed ID: 6759917
TI Inelastic electron tunneling spectroscopic study of interaction of acetylcholine and beta-methyl acetylcholine with alumina surface.
AU Aslanian D; de Cheveigne S
SO Molecular pharmacology, (1982 Nov) Vol. 22, No. 3, pp. 678-86. Journal code: 0035623. ISSN: 0026-895X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198303
ED Entered STN: 19900318
Last Updated on STN: 19990129
Entered Medline: 19830324
AB The conformation of acetylcholine (Ach) and its muscarinic analogue beta-methyl acetylcholine (beta-MeAch) on an alumina surface was analyzed by inelastic electron tunneling spectroscopy (IETS). This method detects vibrational modes of organic molecules that are active in both Raman (R) and IR spectroscopies. By using previously recorded and interpreted R and IR spectra of Ach and beta-MeAch in solid-state and aqueous solutions we studied the perturbations due to adsorption. The results were used to interpret the interaction of both molecules with the alumina surface, and a comparison to that with receptors or with acetylcholinesterase was attempted. In the case of nonhydrolytic interaction, the positive trimethylammonium groups of both molecules seemed to be attracted by the negative oxygen ions of the surface. There was evidence that the O--C--C--N skeleton of Ach changed its conformation in aqueous solution and adopted the solid-state conformation, which is very similar to that of beta-MeAch. This conformation once established, Ach appeared to interact with the alumina surface in the same way as did beta-MeAch: both tunneling spectra were very similar. There was also evidence that in the acetyl part of both molecules the C=O double bond was broken and that the oxygen atom coordinated with an Al+ cation. The acetyl skeleton did not show important conformational changes for either molecule. In the case of hydrolytic interaction of Ach or beta-MeAch, the products of the hydrolysis, acetate ion and choline--the latter also adsorbed in ionic form--were found on the alumina surface. In both cases the conformation of the lateral groups bonded to the choline and acetyl skeletons was also analyzed.

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---Logging off of STN---

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Executing the logoff script...

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	16.20	16.41

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